195 Serum Potassium

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Definition

Potassium, a metallic inorganic ion with atomic weight of 39, is the most abundant cation in the body. The vast majority of potassium is in the intracellular compartment with a small amount in the extracellular space. Normal serum potassium is 3.5 to 5.5 mEq/L; however, plasma potassium is 0.5 mEq/L lower. While total body potassium is lower in females and in older patients, serum potassium concentration is independent of sex and age.

Technique

Serum potassium is measured by the use of a flame photometer or ion-selective electrode. The procedure is rapid, simple, and reproducible. In interpreting serum potassium, it should be kept in mind that because the intracellular potassium concentration is approximately fortyfold greater than the extracellular concentration, any maneuver that would result in the release of a small amount of intracellular potassium will erroneously raise serum potassium. These include: (1) tight tourniquet; (2) vigorous exercise of the extremity during blood drawing; (3) hemolysis due to vigorous shaking of the test tube; (4) thrombocytosis (platelet count greater than 600,000); and (5) leukocytosis (WBC greater than 200,000). In the last two situations, the longer the blood stands, the greater the rise in serum potassium will be.

Basic Science

Total body potassium is approximately 55 mEq/kg body weight. Of this amount, 98% is in the intracellular compartment (primarily in the muscle, skin, subcutaneous tissue, and red blood cells) and 2% is in the extracellular compartment. Therefore in a 70-kg man with total body potassium of 3750 mEq, approximately 3675 mEq is in the intracellular and 75 mEq is in the extracellular space (Figure 195.1). The intracellular potassium concentration is on average 150 mEq/L. The ratio of intracellular to extracellular potassium (K_i:K_e) is the major determinant of the resting membrane potential and plays a crucial role in the normal functioning of all cells, specially those with inherent excitability. This very high concentration difference is maintained by Na-K-ATPase enzyme that actively pumps potassium into the cell while moving sodium out of the cell.

As Figure 195.1 shows, a normal dietary intake of potassium is approximately 100 mEq per day, which is counterbalanced by the excretion of 100 mEq through the kidney and the gut. Humans and other animals are exposed to intermittent high potassium intake, which could increase the extracellular potassium abruptly, resulting in a major change in K_i:K_e ratio with potentially disastrous consequences. To prevent this, most of the potassium is initially shifted into the cell where it is added to the large intracellular pool, without changing the ratio significantly until the kidney is able to excrete the dietary load.

The following factors are important to the internal regulation of potassium.

Factors that shift potassium into the cell:

- Insulin
- Catecholamines
- Aldosterone
- Alkalemia

Factors that shift potassium out of the cell:

- Increase in osmolality
- Acidemia

Insulin secretion, which is stimulated by an increase in serum potassium, shifts the potassium into the liver and muscle cells. Catecholamines, through stimulation of beta-2 receptors, are also able to shift potassium into the cell. Aldosterone is stimulated by a rise in serum potassium, has minimal effect on potassium distribution between intracellular and extracellular compartments. Insulin and catecholamines are not only important in the normal regulation of potassium but when given exogenously in physiologic or pharmacologic doses, can change potassium distribution significantly. Acid–base balance and plasma osmolality are not the usual physiologic regulators but have a potent influence on the potassium distribution. Acid–base balance affects serum potassium by the exchange of hydrogen ions for potassium across the cell membrane. A rise in the serum pH (decrease in H^+ concentration) will result in a shift of H^+ out of the cell and potassium into the cell. The reverse occurs during acidemia with a shift of potassium out of the cell. A sudden increase in plasma osmolality will shift water out of the cell

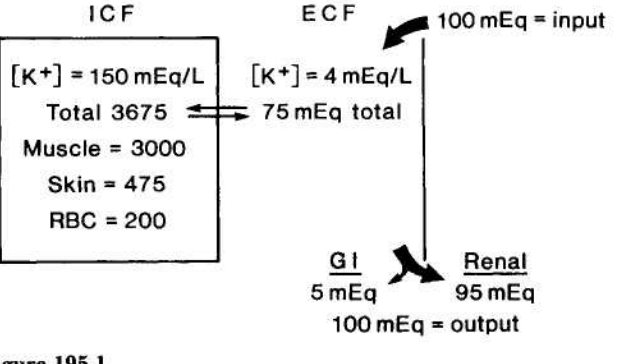

Figure 195.1
Normal potassium homeostasis.

and drag some potassium with the water. This will result in a significant rise in serum potassium.

Long-term potassium homeostasis is maintained by the kidney. Potassium is freely filtered and then 90% reabsorbed in the tubular segments proximal to the distal convoluted tubule. This is independent of potassium intake and final urinary potassium. The majority of the potassium excreted is secreted by specialized cells in the distal convoluted tubule and/or cortical and outer medullary collecting ducts (Figure 195.2). Under severe potassium deprivation, the collecting duct can reabsorb potassium; however, urinary potassium never approaches zero, and therefore there is an obligatory potassium loss of 10 to 15 mEq/day. The factors influencing potassium secretion (and therefore excretion) are:

- Potassium intake
- Intracellular potassium concentration
- Distal delivery of sodium
- Urine flow rate
- Mineralocorticoid activity
- Tubular responsiveness to mineralocorticoids

Aldosterone plays a pivotal role in this process. Humans can adapt to an increase in dietary potassium by an increase in the renal excretion of this ion; therefore, high dietary potassium should not lead to hyperkalemia in normal subjects.

Clinical Significance

The normal range for serum potassium is narrow (3.5 to 5.5 mEq/L), and minor departure from this range (by less than 1.0 mEq/L) is associated with significant morbidity and mortality. Although a 1.0 mEq change in concentration is small in absolute terms, it changes the K_i:K_e ratio by 25%. Therefore rapid evaluation and, when indicated, treatment of hypo- and hyperkalemia are critical. Table 195.1 summarizes the clinical consequence of hypo- and hyperkalemia. These symptoms, signs, and laboratory findings should alert the clinician to the possible existence of a significant derangement in serum potassium. Neuromuscular and cardiac signs and symptoms can be quite similar and can include nonspecific minor complaints (e.g., weakness, tiredness, and palpitation), as well as major symptoms (paralysis and sudden death). As indicated in Table 195.1, hypokalemia can also present with gastrointestinal, metabolic, and renal abnormalities.

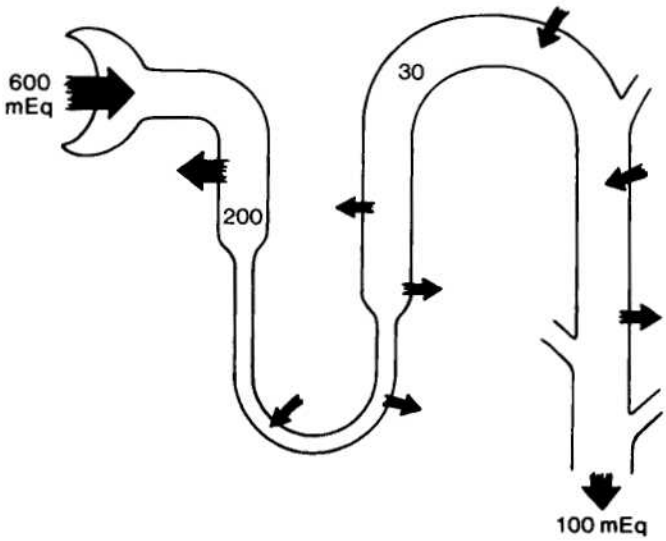

Figure 195.2
Renal handling of potassium.

Table 195.1
Clinical Consequences of Hypo- and Hyperkalemia

	Hypokalemia	Hyperkalemia
Neuromuscular	Weakness Paralysis	Weakness Paralysis
Cardiac	Arrhythmia ECG: U wave	Arrhythmia ECG: peaked T wave
Gastrointestinal	Ileus	—
Metabolic	Hyperglycemia ↑ NH_3 production	— ↓ NH_3 production
Renal	Polyuria	

Hypokalemia

Serum potassium concentration does not always reflect total body potassium; therefore, hypokalemia could coexist with both normal or low total body potassium (see Table 195.3).

Hypokalemia with normal total body potassium, by definition, is due to a shift of potassium into the cell. This shift could occur in alkalemia, states of high endogenous or exogenous insulin or catecholamines, and, in very rare situations, for unknown reasons (hypokalemic periodic paralysis). In clinical practice, alkalemia is the most common cause of hypokalemia. Table 195.2 indicates the extent of expected changes in serum potassium with alkalemia of either respiratory or metabolic origin. The figure of 0.25 mEq/L per 0.1 U increase in pH could be used to correct the measured serum potassium.

Hypokalemia without intracellular shift of potassium is seen only when there is marked potassium deficiency. As an approximation, a 1.0 mEq/L decrease in serum potassium is associated with a deficit of 200 to 300 mEq, while a 2.0 mEq/L decrease is associated with a 500 to 600 mEq deficit in total body potassium. It should be noted that any judgment regarding the state of total body potassium is, at

Table 195.2
Approximate Changes in Serum Potassium Associated with Acid–Base Disturbances

Pathologic process	Direction	Amount (mEq/L per 0.1 unit pH change)
Acidemia (pH <7.35)		
Metabolic acidosis		
Mineral acidosis	Increase	1.0
Organic acidosis	No change	—
Respiratory		0.20
Alkalemia (pH >7.45)		
Metabolic alkalosis	Decrease	0.25
Respiratory alkalosis	Decrease	0.25

Table 195.3
Etiology of Hypokalemia

With normal total body potassium
Alkalemia
↑ insulin (exogenous or endogenous)
↑ catecholamines (exogenous or endogenous)
Unknown (hypokalemic periodic paralysis)
With low total body potassium
Poor intake
Increased loss
Skin
Gastrointestinal
Renal
Rapid cellular proliferation

best, a gross approximation, and one should utilize all historical, physical, and laboratory information available to make this approximation more accurate. As Table 195.3 indicates, hypokalemia associated with a low total body potassium is either due to poor dietary intake or increased potassium loss from the body. Poor intake is an uncommon cause, for most foods contain some potassium. Nevertheless, patients with extremely poor dietary intake (most commonly alcoholics) and patients on severe weight-reduction programs are in danger of developing severe potassium deficiency. Hypokalemia due to an increase in potassium loss is most commonly secondary to gastrointestinal disorders. Although the potassium content of gastrointestinal fluids is quite low (Table 195.4), the resultant dehydration stimulates aldosterone production, which increases urinary potassium significantly. The renal potassium wasting continues as long as dehydration persists. If gastrointestinal fluid loss is from the stomach, hypokalemia is partly due to intracellular shift of potassium secondary to alkalemia and partly due to increased renal potassium loss due to high aldosterone level. Sweat contains only a small amount of potassium, and excess sweating is rarely the cause of significant hypokalemia.

Renal potassium loss is most commonly associated with a high aldosterone level (either as a primary or secondary event). The most common cause of renal potassium wastage is the use of diuretics that induce kaliuresis through several mechanisms (including increase in aldosterone level, increase in urine volume, increase in the delivery of sodium to the exchange sites, hypochloremia, and metabolic alkalosis). Less commonly, renal potassium wasting results from a primary increase in circulating mineralocorticoids, such as occurs in Cushing's syndrome or primary hyperaldosteronism.

Table 195.4
Potassium Content of Body Fluid

Fluid	Amount (L)	Concentration (mEq/L)	Total (mEq/24 hr)
Sweat	0.4	10	4
Saliva	1.0	10–20	10–20
Gastric	1.0–2.0	5–10	10–20
Pancreatic	1.0–2.0	5	5–10
Small bowel	1.0–2.0	5	5–10
Stool	0.1	20–130	7–15

As noted, urinary potassium excretion tends to be elevated in the gastrointestinal as well as the renal causes of hypokalemia. However, the urine potassium is usually below 20 mEq/L in the former and above 20 mEq/L in the latter. The most critical data to differentiate these two large groups are historical (e.g., history of vomiting, diarrhea, or diuretic use) and physical data (blood pressure, pulse, and other volume parameters). More sophisticated laboratory studies are often needed to reach a specific diagnosis in either category.

Hyperkalemia

Serum potassium above 5.5 mEq/L should be worked up rapidly and treated appropriately. Serum potassium above 6.5 mEq/L is associated with significant morbidity and mortality and should be handled as an emergency.

Table 195.5 categorizes hyperkalemia into three groups: pseudohyperkalemia, hyperkalemia with normal total body potassium, and hyperkalemia with high total body potassium.

Pseudohyperkalemia signifies an in vitro phenomenon (i.e., the in vivo serum potassium is normal). This is caused by the release of potassium from cellular components of blood during the process of clotting and, less commonly, by the release of potassium from ischemic muscle cells due to tight tourniquet or hand/arm exercise during the blood-drawing process. If the latter is suspected, blood should be drawn in a proper manner again and serum potassium repeated. If the former is suspected, the platelet and white cell counts should be checked, and serum should be inspected for significant hemolysis. Hyperkalemia occurs when there is thrombocytosis (platelet count greater than 600,000), leukocytosis (WBC greater than 200,000) or significant hemolysis (serum hemoglobin greater than 1.5 g/dl). If thrombocytosis or severe leukocytosis is present, then plasma potassium should be measured. If hemolysis is present, blood drawing should be carefully repeated.

Hyperkalemia with normal total body potassium is caused by the shift of potassium out of the cell and is commonly seen in acidemia, sudden increase in plasma osmolality, massive tissue breakdown and, in very rare circumstances, adrenergic blockade and hyperkalemic periodic paralysis (Table

Table 195.5
Etiology of Hyperkalemia

Pseudohyperkalemia
Hemolysis (in vitro)
Leukocytosis
Thrombocytosis
With normal total body potassium
Acidemia
Beta adrenergic blockade
↑ plasma osmolality
Massive cell breakdown (in vivo hemolysis, rhabdomyolysis)
Unknown (hyperkalemic periodic paralysis)
With increased total body potassium
Increased intake
Decreased output
GFR <20 ml/min
Decreased renal secretion (GFR >20 ml/min)
Low aldosterone level
Normal aldosterone level

195.5). Acidemia is by far the most important cause of hyperkalemia. As Table 195.2 shows, mineral acidosis (e.g., renal failure acidosis) is associated with the greatest shift (1.0 mEq/L for each 0.1 U decrease in pH) of potassium, whereas organic acidosis (e.g., lactic acidosis) is associated with little or no change. Respiratory acidosis results in a modest shift (0.2 mEq/L for each 0.1 pH change). These figures, while approximate, can be used to correct the measured serum potassium. Beta blockade can result in significant hyperkalemia during and immediately after exercise. This is because the potassium initially released from the muscle cells is normally taken up by these cells through the stimulation of beta-2 receptors by catecholamines. A sudden rise in osmolality can result in a modest increase in serum potassium (0.3 to 0.5 mEq/L); this rise, however, can be much greater in diabetic patients, who lack normal insulin and aldosterone responses to hyperkalemia.

Hyperkalemia with increase in total body potassium is almost always caused by a decrease in renal excretion of potassium and is rarely the result of an increase in intake alone. Patients with normal kidney function can adapt to increase in potassium intake unless the potassium is given rapidly (e.g., intravenous infusion) or is given to a patient with a renal defect in potassium excretion.

A decrease in renal potassium excretion is either primary renal in origin or caused by a defect in the renin-angiotensin-aldosterone axis. Although potassium excretion is primarily a secretory phenomenon, marked decreases in glomerular filtration rate (GFR) to below 20 ml/min can be associated with hyperkalemia. In patients with relatively normal GFR, hyperkalemia is usually due to a defect in the renin-angiotensin-aldosterone axis or to a defect in the renal tubular responsiveness to aldosterone. In these patients, measurement of plasma aldosterone level and, if needed, further evaluation of the renin-angiotensin-aldosterone axis may be required for definitive diagnosis.

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